REMARKS

Claims 4-9 are pending and have been examined on the merits and claims 13-18 are added hereinabove. Support for the subject matter of new claims 13-18 can be found in the specification, page 9, first paragraph, on figure 4 and on the subject matter of claims 4-9. No new matter has been added.

In the Office Action, claims 4-9 have been rejected under 35 U.S.C. § 103(a) as being obvious over Root et al. (Journal of General Virology, 2000, hereinafter "Root") in view of Stewart et al. (Biochemistry, 1999, hereinafter "Stewart") and Heredia et al. (Journal of Acquired Immune Deficiency Syndrome, 2000, hereinafter "Heredia") Applicants respectfully traverse these rejections.

The presently claimed invention is directed to methods for inhibiting influenza virus replication and for treating influenza virus infection by administering an effective amount of resveratrol. In addition, the presently claimed invention is directed to methods for non-reversibly inhibiting influenza virus replication and treating influenza virus infection of a non-reversibly inhibited influenza virus by administering an effective amount of resveratrol (*e.g.*, from page 8 line 21, to page 9 line 14).

Root does not disclose Applicants' invention. Root only describes that a highly specific protein kinase C ("PKC") inhibitor such as bisindolylmaleimide is capable of inhibiting the entry of influenza viruses into target cells (*e.g.*, page 2698, last two lines of column 1, to line 2 of column 2). However, Root teaches that not all the viruses behave similarly with regard to binding and entry into target cells, even if they belong to the same family of viruses (*e.g.*, page 2697, col. 1 lines 6-11). Moreover, Root discloses that certain PKC inhibitors (*e.g.*, H7 and staurosporine) interfere with the entry mechanisms

of several viruses, such as rhabdoviruses, alphaviruses, poxviruses and herpesviruses, require PKC activity. However, these very same PKC inhibitors have been reported to have no effect on cell entry of orthomixyxoviruses, such as influenza virus (*e.g.*, page 2698, col. 1, lines 27-38). Further, the data disclosed in Root confirmed that bisindolylmaleimide I reversibly inhibits virus entry into the cells (*e.g.*, page 2701, col. 2, lines 10-13 and lines 47-50, and from page 2701 line 51 to page 2703, col. 1, line 2). As such, Root does not disclose, teach or even suggest the presently claimed methods of inhibiting influenza virus replication with the PKC inhibitor resveratrol.

As an initial matter, Root is completely silent with regard of using resveratrol. Second, Root discloses that not all the viruses behave in the same way. Third, Root discloses that only a highly specific PKC inhibitor such as bisindolylmaleimide 1. HCl is capable of blocking the entry, but not the replication, of the influenza virus. In addition, it discloses that several PKC inhibitors are virus specific. In other words, they are capable of inhibiting the entry mechanisms of certain viruses but not of others. And finally, Root teaches that the action of bisindolylmaleimide is reversible.

Stewart also does not disclose Applicants' claimed subject matter and does not make up for Root' s deficiency in that it suffers from the same defects.

Stewart teaches and discloses the anti-cancer activity of resveratrol (*e.g.*, page 13244, col. 1, lines 3-4). According to Stewart there is provided that the tumor antagonism of resveratrol cannot be based on its PKC inhibitory activity because resveratrol is a very weak PKC inhibitor (*e.g.*, page 13245, col. 1, lines 3-9). Stewart discloses that because resveratrol is a weak PKC inhibitor, the dosage required would be highly toxic to mammalian cells and not relevant to its chemoprotective properties.

Steward concluded by saying that the PKC inhibitory activity of resveratrol is not worth it being pursued in this line of investigation.

Accordingly, for the reason set forth above, Root and Stewart, alone or in combination, discloses the claimed subject matter. Further, it is submitted that there is no motivation to combine their teachings to arrive at the presently claimed invention. On the contrary, the combination of the two references teaches away from the presently claimed invention. Namely, Root discloses that only a very specific PKC inhibitor can block the influenza virus entry into the target cells. On the other hand, Stewart discloses that resveratrol is a very weak PKC inhibitor against a broad spectrum of protein kinases (*e.g.*, it is not very specific).

Heredia also does not teach Applicants' claimed invention and does not correct Root's and Stewart's deficiencies in that it also suffers from the same defects.

As previously submitted, Heredia teaches that resveratrol synergistically inhibits HIV replication (*e.g.*, summary, lines 3-5). However, as also previously submitted and as cited by the Examiner on page 3 of the current Office Action, HIV and influenza are distinct RNA viruses, possessing different life cycle. Thus, one of ordinary skill in the art would not reasonable expect that a treatment for HIV would necessarily treat influenza and vice versa.

As such, Applicants respectfully disagree with the Examiner's statement on page 5, point 11 of the Office Action in which it is said that resveratrol is a natural "widely used natural product" indicating that it is already safely used , in vivo, and can be obtained at a low-cost. This statement does not provide the motivation for a skilled artisan to combine the teachings of Root with Stewart. The fact that resveratrol can be

used in vivo and that it is low cost is irrelevant with regard to the motivation to combine Root with Stewart.

As set forth above, Root stand for the proposition of inhibiting viral entry into the target cells with a very specific PKC inhibitor. Stewart is completely silent with regard of viruses and only discloses a compound whose very weak PKC inhibition cannot even account for its anti-tumor activity. Thus, none of the three references, alone or in combination, teaches using resveratrol to inhibit influenza virus replication and influenza virus treatment.

Accordingly, it is respectfully submitted that the cited references failed to render obvious the subject matter of claims 4-9 and 13-18. Thus, withdrawal of the rejection of claims 4-9 and 13-18 as being obvious under 35 U.S.C. § 103 (a) over Root in view of Stewart and Heredia is respectfully requested.

Accordingly, it is submitted that all of the pending claims are now in conditions for allowance and a Notice to that effect is earnestly solicited.

This response is being filed within the shortened statutory period for response, thus, no fees are believed to be due. If, on the other hand, it is determined that further fees are necessary or any overpayment has been made, the Commissioner is hereby authorized to debit or credit such sum to Deposit Account No. 02-2275.

Pursuant to 37 C.F.R. § 1.136(a), please treat this and any concurrent or future reply in this application that requires a petition for an extension of time of its timely submission as incorporating a petition for extension of time for the appropriate length of time. The fee associated herewith is to be charged to the above-mentioned deposit account.

An early and favorable action on the merits is earnestly solicited.

Respectfully submitted

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